SARS-CoV-2 incidence and vaccine escape

AUTHORS

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A recent Editorial[1] described the potential for the evolution of SARS-CoV-2 variants that render vaccines less effective (vaccine escape), assisted by waning immunity following vaccination. This raises a crucial question: how can COVID-19 exit strategies be planned with only a low vaccine escape risk?

A key component of any plausible strategy towards the permanent removal of non-pharmaceutical interventions (NPIs) involves ensuring low case numbers in the short-to-mid-term using NPIs and vaccination. Assuming a fixed vaccine escape mutation probability per infection (p), the risk of a vaccine escape variant arising in a specified time period is

$$\text{Prob}(\text{vaccine escape}) = 1 - (1 - p)^N,$$

where N represents the number of cases in that period.

Crucially, this indicates that the vaccine escape risk is sensitive to background incidence: the risk of an escape variant appearing within a fixed time is an increasing function of incidence (Fig 1). Reducing cases is not only beneficial for decreasing the pressure on healthcare systems, but also for lowering the vaccine escape risk.

Of course, there are fundamental differences between using NPIs and vaccines to lower incidence. When considering vaccines that do not prevent transmission entirely, there is an interplay between reduced cases at the population-level and the potential for selection for vaccine escape variants in infected vaccinated hosts[2–4]. A related question is whether it is most beneficial to vaccinate many individuals using single vaccine doses or fewer individuals twice. “Dose-sparing” strategies could in theory lead to selection for vaccine escape variants[5]. However, current evidence suggests tentatively that the net vaccine escape risk is lower when more hosts are vaccinated with single doses, due to reduced cases[2].

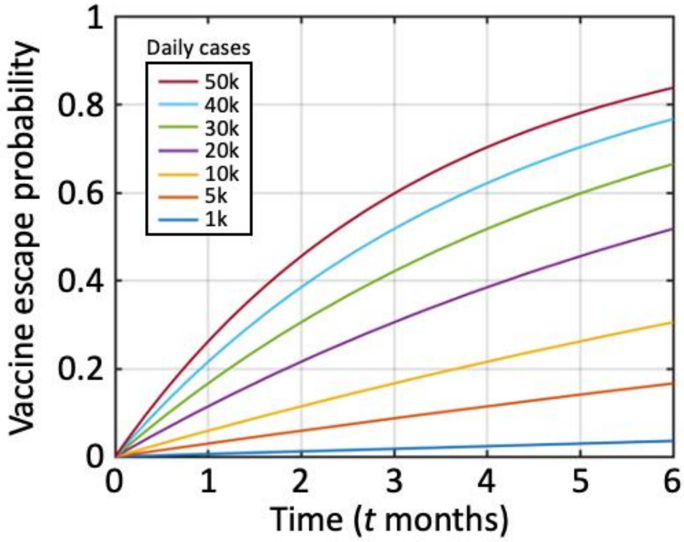

Figure 1. The risk that at least one vaccine escape variant arises in a time period of length t, for different daily numbers of cases. In this figure, the per infection probability of vaccine escape is $p = 2 \times 10^{-7}$ (for details, see Supplementary Material).

Despite its simplicity, our quantitative illustration demonstrates that strategies for mitigating the vaccine escape risk should be explored. Reducing case numbers locally should only be one component of these strategies. Travel restrictions to reduce the risk of importing novel variants should be considered. We recognise that assessing the escape variant emergence risk not only requires the variant to arise via mutation as considered here, but also to grow to appreciable frequencies. This is a stochastic process, depending on the availability of hosts to infect and the escape variant's fitness. A reduction in cases leads to both a reduction in the risk of escape variants appearing and a reduction in their subsequent establishment through transmission around the population. Acquisition of additional mutations that are beneficial for the virus is also more likely to be suppressed if incidence rates are reduced.

In summary, high SARS-CoV-2 incidence rates act to increase the vaccine escape risk. Maintaining low case numbers using NPIs and vaccines is critical at the current time.

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